Clinical trial results:
Multicentric randomized phase III trial comparing 6-month adjuvant chemotherapy with gemcitabine versus 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin (mFolfirinox) in patients with resected pancreatic adenocarcinoma.

Summary

EudraCT number	2011-002026-52
Trial protocol	FR
Global end of trial date	16 July 2021

Results information

Result version number	v1 (current)
This version publication date	04 November 2023
First version publication date	04 November 2023

Trial information

Trial identification

Sponsor protocol code	UC 0110/1006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01526135
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UNICANCER
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75013
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 April 2018
Global end of trial reached?	Yes
Global end of trial date	16 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare disease-free survival (DFS) at 3 years between the experimental (mFOLFIRINOX) and control arms (gemcitabine).

Protection of trial subjects:

This study was conducted in accordance with the Declaration of Helsinki (1964) and subsequent amendments, ICH Good Clinical Practice (GCP) Guidelines (CPMP/ICH/135/95), the European Directive (2001/20/CE) and the applicable local regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 April 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 400
Country: Number of subjects enrolled	Canada: 93
Worldwide total number of subjects	493
EEA total number of subjects	400

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	306
From 65 to 84 years	187

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The Prodige 24 – Accord 24 study randomized 493 patients between 16-Apr-2012 and the 03-Oct-2016: 400 patients in France and 93 in Canada.
Overall, 85 centers were initiated of which 77 included patients: 58 centers in France and 19 in Canada.

Pre-assignment

Screening details:

The study consisted of a screening phase before randomization to establish eligibility. The maximum duration of treatment in both study arms was 6 months, and a long-term follow-up.
The endpoint evaluated (DFS, OS, specific survival, MFS, and safety according to NCI CTCAE v4.0).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Gemcitabine

Arm description:

Standard treatment:
Gemcitabine (1000 mg/m²) was administered intravenously over 30 min, once weekly for three weeks followed by one week of rest (one 4-week treatment cycle = 3 weeks of gemcitabine administered weekly then one week of rest). Treatment duration was planned for 6 cycles (24 weeks).

Arm type	Standard
Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intracavernous use

Dosage and administration details:

Gemcitabine (1000 mg/m²) was administered intravenously over 30 min, once weekly for three weeks followed by one week of rest (one 4-week treatment cycle = 3 weeks of gemcitabine administered weekly then one week of rest). Treatment duration was planned for 6 cycles (24 weeks).

Arm title	mFOLFIRINOX

Arm description:

Experimental treatment:
mFOLFIRINOX administered as 2-week cycles. On day (D)1 of each cycle, oxaliplatin (85 mg/m2) was administered by IV infusion over 2 h. Followed by racemic folinic acid/leucovorin (400 mg/m2) or L-folinic acid (200 mg/m2) as a 2-h IV infusion. After 30 min of the folinic acid infusion, irinotecan (180 mg/m2) was infused intravenously, via a Y-connector, over 90 min. This was followed by a continuous infusion over 46 h of 5-FU (2400 mg/m2). The starting dose of irinotecan was reduced to 150 mg/m2 during after a planned safety analysis.

Arm type	Experimental
Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: Oxaliplatin (Eloxatin®) 85 mg/m² D1 over 2 hours.	
Investigational medicinal product name	rinotecan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Irinotecan (Campto®) 180 mg/m²/150 mg/m² (on D1 over 90 min to begin 30 min after starting the folinic acid infusion.). The initial irinotecan dose was reduced from 180 mg/m2 to 150 mg/m² following the IDMC held on the 12-Mar-2014. The protocol was modified by amendment N°7	
Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 5-FU 2.4 g/m² IV continuous infusion over 48 hours (1200 mg/m²/ day).	
Investigational medicinal product name	Folinic acid (racemate) or Lfolinic acid (enantiomer)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 400 mg/m2 (racemate) or 200 mg/m2 (enantiomer) (IV infusion over 2 h).	

Number of subjects in period 1	Gemcitabine	mFOLFIRINOX
Started	246	247
Completed	192	158
Not completed	54	89
Relapse	26	15
Physician decision	2	7
Patient decision	2	13
Toxicity	11	21
Intercurrent disease	2	1
Wrongly inclusion	-	2
Missing data	8	21
Patients randomized but not treated	3	9

Baseline characteristics

Reporting groups	
Reporting group title	Gemcitabine

Reporting group description:

Standard treatment:
Gemcitabine (1000 mg/m²) was administered intravenously over 30 min, once weekly for three weeks followed by one week of rest (one 4-week treatment cycle = 3 weeks of gemcitabine administered weekly then one week of rest). Treatment duration was planned for 6 cycles (24 weeks).

Reporting group title	mFOLFIRINOX

Reporting group description:

Experimental treatment:
mFOLFIRINOX administered as 2-week cycles. On day (D)1 of each cycle, oxaliplatin (85 mg/m2) was administered by IV infusion over 2 h. Followed by racemic folinic acid/leucovorin (400 mg/m2) or L-folinic acid (200 mg/m2) as a 2-h IV infusion. After 30 min of the folinic acid infusion, irinotecan (180 mg/m2) was infused intravenously, via a Y-connector, over 90 min. This was followed by a continuous infusion over 46 h of 5-FU (2400 mg/m2). The starting dose of irinotecan was reduced to 150 mg/m2 during after a planned safety analysis.

Reporting group values	Gemcitabine	mFOLFIRINOX	Total
Number of subjects	246	247	493
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	147	159	306
From 65-84 years	99	88	187
85 years and over	0	0	0
Age continuous Units: years			
median	64	63	
full range (min-max)	30 to 81	30 to 79	-
Gender categorical Units: Subjects			
Female	111	105	216
Male	135	142	277
ECOG PS Units: Subjects			
ECOG 0	127	122	249
ECOG 1	115	123	238
Missing data	4	2	6
Tumor location Units: Subjects			
Head	166	188	354
Head except hook	9	5	14

Hook	5	3	8
Isthmus	5	5	10
Body	15	13	28
Tail	29	21	50
Other	13	11	24
Missing	4	1	5
Dealy from primary tumour diagnosis to randomisation			
Units: Months			
median	1.6	1.6	
full range (min-max)	0.3 to 6.1	0.1 to 2.9	-
Time between surgery and inclusion			
Units: Months			
median	1.8	1.8	
full range (min-max)	0.7 to 3.1	0.8 to 2.9	-

End points

End points reporting groups

Reporting group title	Gemcitabine

Reporting group description:

Standard treatment:
Gemcitabine (1000 mg/m²) was administered intravenously over 30 min, once weekly for three weeks followed by one week of rest (one 4-week treatment cycle = 3 weeks of gemcitabine administered weekly then one week of rest). Treatment duration was planned for 6 cycles (24 weeks).

Reporting group title	mFOLFIRINOX

Reporting group description:

Experimental treatment:
mFOLFIRINOX administered as 2-week cycles. On day (D)1 of each cycle, oxaliplatin (85 mg/m2) was administered by IV infusion over 2 h. Followed by racemic folinic acid/leucovorin (400 mg/m2) or L-folinic acid (200 mg/m2) as a 2-h IV infusion. After 30 min of the folinic acid infusion, irinotecan (180 mg/m2) was infused intravenously, via a Y-connector, over 90 min. This was followed by a continuous infusion over 46 h of 5-FU (2400 mg/m2). The starting dose of irinotecan was reduced to 150 mg/m2 during after a planned safety analysis.

Primary: Disease-free survival (DFS)

End point title	Disease-free survival (DFS)

End point description:

Disease free survival (DFS) is defined as the interval between randomization and the occurrence of the first observed oncologic event, such as, local, metastatic recurrence, second cancer, or death from any cause. Patients without event at the time of analysis will be censored on the date of the last informative follow-up.

End point type	Primary

End point timeframe:

3 years after randomization.

End point values	Gemcitabine	mFOLFIRINOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Months				
median (confidence interval 95%)	12.8 (11.7 to 15.2)	21.6 (17.7 to 27.6)		

Statistical analyses

Statistical analysis title	DFS analysis
Comparison groups	mFOLFIRINOX v Gemcitabine

Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	0.73

Secondary: Overall survival

End point title	Overall survival

End point description:

Overall survival is the time delay between the date of randomization and the patient’s death, irrespective of its cause. Patients who are still living at the time of analysis will be censored at the date of last follow-up visit.

End point type	Secondary

End point timeframe:

From randomisation to death, up to 5 years.

End point values	Gemcitabine	mFOLFIRINOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Months				
median (confidence interval 95%)	35.5 (30.1 to 40.3)	53.5 (43.5 to 58.4)		

Statistical analyses

Statistical analysis title	OS analysis
Comparison groups	Gemcitabine v mFOLFIRINOX
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.85
Variability estimate	Standard deviation

Secondary: Specific survival

End point title	Specific survival

End point description:

Specific survival is the time delay between the date of randomization and the patient’s death due to the treated cancer or a treatment-related complication.

End point type	Secondary

End point timeframe:

From randomisation to death, up to 5 years.

End point values	Gemcitabine	mFOLFIRINOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Months				
median (confidence interval 95%)	36.3 (30.5 to 43.9)	54.7 (45.8 to 68.4)		

Statistical analyses

Statistical analysis title	Specific survival analysis
Comparison groups	Gemcitabine v mFOLFIRINOX
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.82

Secondary: Metastasis-free survival (MFS)

End point title	Metastasis-free survival (MFS)

End point description:

Metastasis-free survival is the time delay between the date of randomization and the date of the 1st distant event occurrence (peritoneal, hepatic, pulmonary, and lymph nodes). Loco-regional progression were not considered as events. Patients still living without metastasis at the time of analysis were to be censored at the date of last follow-up examination objectively assessing this type of event.

End point type	Secondary

End point timeframe:

36 Months

End point values	Gemcitabine	mFOLFIRINOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Months				
median (confidence interval 95%)	17.7 (14.0 to 21.2)	29.4 (21.4 to 40.1)		

Statistical analyses

Statistical analysis title	MFS analysis
Comparison groups	Gemcitabine v mFOLFIRINOX
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	0.8
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From inclusion until 30 days after end of treatment (up to 5 years).

Adverse event reporting additional description:

Only subjects affected number is available. in the table of value for non serious AE only subjects affected number is reported (Occurences not available).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14

Reporting groups

Reporting group title	Gemcitabine
Reporting group description: -	
Reporting group title	mFOLFIRINOX

Reporting group description: -

Serious adverse events	Gemcitabine	mFOLFIRINOX	
Total subjects affected by serious adverse events			
subjects affected / exposed	58 / 246 (23.58%)	92 / 247 (37.25%)	
number of deaths (all causes)	114	92	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer			

subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melanoma			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine carcinoma			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal cancer			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary carcinoma			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
catheter thrombosis			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
femoral artery thrombosis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischemic stroke			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboembolic event			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischemic attack			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Anasarca			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			

subjects affected / exposed	0 / 246 (0.00%)	4 / 247 (1.62%)	
occurrences causally related to treatment / all	0 / 0	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug delivery system malfunction			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Edema			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 246 (0.81%)	3 / 247 (1.21%)	
occurrences causally related to treatment / all	1 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema lower limb			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contrast media reaction			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug allergy			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
dyspnea			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial pneumonitis			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight loss			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Biliary anastomosis complication			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion site extravasation			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leg injury			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perforation of anastomosis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Fahr's disease			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary spasm			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non ST segment elevation myocardial infarction			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial thrombosis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphonia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cholinergic syndrome			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysesthesia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epileptic seizure			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy			
subjects affected / exposed	0 / 246 (0.00%)	5 / 247 (2.02%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurotoxicity			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paresthesia			
subjects affected / exposed	0 / 246 (0.00%)	4 / 247 (1.62%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensory peripheral neuropathy			

subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue paralysis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasovagal reaction			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 246 (1.22%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplasia bone marrow			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile aplasia			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	3 / 246 (1.22%)	4 / 247 (1.62%)	
occurrences causally related to treatment / all	3 / 3	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	4 / 246 (1.63%)	6 / 247 (2.43%)	
occurrences causally related to treatment / all	4 / 4	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenic purpura			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal abscess			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic ulcer			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowel obstruction			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	1 / 246 (0.41%)	12 / 247 (4.86%)	
occurrences causally related to treatment / all	1 / 1	13 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal obstruction			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal bleeding			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 246 (0.00%)	5 / 247 (2.02%)	
occurrences causally related to treatment / all	0 / 0	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroparesis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemorrhoidal crisis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernial eventration			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypogastric pain			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	4 / 246 (1.63%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic abscess			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Protein-losing gastroenteropathy			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
sigmoiditis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subocclusive syndrome			
subjects affected / exposed	2 / 246 (0.81%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Upper gastrointestinal bleeding			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
hepatic function disorder			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Icterus			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute renal failure			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
calf pain			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cervical pain			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis fracture			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteremia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial translocation			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter related infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Escherichia coli infection			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection pseudomonas aeruginosa			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pneumonitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nocardiosis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis perforative			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
shock septic			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Serratia infection			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylodiscitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcus epidermidis infection			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pericarditis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound abscess			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia coli bacteremia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Anorexia			

subjects affected / exposed	1 / 246 (0.41%)	4 / 247 (1.62%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Edema generalized			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of control of diabetes			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	2 / 246 (0.81%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Gemcitabine	mFOLFIRINOX	
Total subjects affected by non-serious adverse events subjects affected / exposed	246 / 246 (100.00%)	247 / 247 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Other-neoplasms subjects affected / exposed occurrences (all)	242 / 246 (98.37%) 242	237 / 247 (95.95%) 237	
Vascular disorders Hypotension subjects affected / exposed occurrences (all)	241 / 246 (97.97%) 241	237 / 247 (95.95%) 237	
Thrombosis/embolism subjects affected / exposed occurrences (all)	241 / 246 (97.97%) 241	237 / 247 (95.95%) 237	
Hypertension subjects affected / exposed occurrences (all)	242 / 246 (98.37%) 242	237 / 247 (95.95%) 237	
Other-vascular disorders subjects affected / exposed occurrences (all)	242 / 246 (98.37%) 242	237 / 247 (95.95%) 237	
Surgical and medical procedures Other-surgical procedures subjects affected / exposed occurrences (all)	242 / 246 (98.37%) 242	237 / 247 (95.95%) 237	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	241 / 246 (97.97%) 241	237 / 247 (95.95%) 237	
Fever subjects affected / exposed occurrences (all)	241 / 246 (97.97%) 241	237 / 247 (95.95%) 237	
Quincke edema			

subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Local reaction at the site of injection			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Edema			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Chills			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Flu-like symptoms			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Pain			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-general disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Immune system disorders			
Immune system disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Reproductive system and breast disorders			
Other-reproductive disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Cough			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Dyspnea			

subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-respiratory disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Anxiety			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Depression			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-psychiatric disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-injury			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Pericarditis			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Chest pain			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-cardiac disorders			

subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Nervous system disorders			
Dizziness			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Dysguesia			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Motor neuropathy			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Paresthesia			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Sensory peripheral neuropathy			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Somnolence			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Headache			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Dysesthesia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Cholinergic syndrome			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Tremor			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-nervous disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	

Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Anaemia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Hyperleucocytosis			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-blood			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Ear and labyrinth disorders			
Hearing			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Tinnitus			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-ear disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Blurry vision			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-eye disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Constipation			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Diarrhea			

subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Mucositis			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Nausea			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Vomiting			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Dyspepsia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Flatulence/bloating			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Hemorrhoids			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Gastro-esophageal reflux			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Epigastric pain			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Stearrhea			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Dysphagia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Xerostomia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-gastrointestinal disorders			

subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Hepatobiliary disorders			
Hepatobiliary disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Cutaneous hyperpigmentation			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Hand-foot cutaneous reaction			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Pruritus			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Rash (redness)			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Rash/desquamation			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Sweating			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Folliculitis			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Erythema			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-cutaneous disorders			

subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Renal and urinary disorders			
Nycturia			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Proteinuria			
subjects affected / exposed	229 / 246 (93.09%)	219 / 247 (88.66%)	
occurrences (all)	229	219	
Other-urinary disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Back pain			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Myalgia			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Pain in extremity			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Shoulder pain			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Neck pain			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Bone pain			

subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-musculoskeletal disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Infections and infestations			
Fissures/ulceration			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Infection without neutropenia			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Local infections			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Paronychia			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Bronchitis/sinusitis/rhinitis			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Urinary infection			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Abscess			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-infections			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	241 / 246 (97.97%)	237 / 247 (95.95%)	
occurrences (all)	241	237	
Hyperglycemia			

subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Hypoglycemia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Diabetes			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Glucose intolerance			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Hypokalemia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Hyperkalemia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Hypoalbuminemia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Hypocalcemia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Hypomagnesemia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Hyponatremia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Hypernatremia			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	
Other-metabolism disorders			
subjects affected / exposed	242 / 246 (98.37%)	237 / 247 (95.95%)	
occurrences (all)	242	237	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 January 2012	-Change of the trial sponsor from the Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) to UNICANCER.
05 January 2012	-Modification of the investigators list.
03 July 2012	-Clarification of the study protocol. -Modification of the investigators list.
06 November 2012	-Modification of the investigators list.
06 May 2013	-Clarification and correction of the protocol -Change in the project leader from Beata JUZYNA to Trevor STANBURY -Change in the name of the statistical unit from CRLC Val d'Aurelle Unité de Biostatistiques CTD INCa to Institut Régional Montpellier du Cancer Montpellier/Val d'Aurelle (ICM), with the subsequent change of the email address of the statistician. -Modification of the investigators list.
08 October 2013	-Modification of the investigators list.
07 October 2014	-Modification of the irinotecan dose from 180 mg/m2 to 150 mg/m2. An interim analysis after the inclusion of 30 patients in the mFOLFIRINOX. If the rate of diarrhea (grade 3-4) 5% the dose of irinotecan would be reduced to 150 mg/m2. Thus, following an IDMC held on the 12-Mar-2014, the protocol was modified to reduce the dose of irinotecan to 150 mg/m2. -Modification of the inclusion criterion N°11, concerning the allowed interval from surgery to initiation of adjuvant chemotherapy. The interval was initially 21 and 70 days and extended to between 21 and 84 days. The publication by Valle et al. showed that the interval from surgery had no impact on the efficacy of adjuvant chemotherapy for treating patients with pancreatic cancer. -Removal of the recommendation for the use of calcium gluconate and magnesium sulfate to prevent oxaliplatin-induced neurotoxicity. A publication by Loprinzi et al. reported that these treatments were not effective in preventing neurotoxicity in colon cancer patients receiving oxaliplatin . -Modification of the contact details. -Modification of the investigators list.
07 April 2015	-Prolongation of the inclusion period by two years (from 3 years to 5 years). -Correction of errors in the protocol. -Modification of the investigators list.
02 February 2016	-Modification of the investigators list.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported